<u>**REMARKS**</u>

A.   Status of the Claims

Claims 1-18 were examined and remain pending. No amendments or cancellations have been made. A clean copy of the pending claims is attached for the Office's convenience at Appendix 1.

B.   The Claims Are Enabled

The Office rejects claims 1-18 under 35 U.S.C. § 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention[.]" March 2004 Office Action at p. 2. The Office has the initial burden to establish a reasonable basis to question the enablement provided for claim 1. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). Applicants respectfully traverse because the Office has not carried its burden for the reasons provided below.

1.   Claim 1

Claim 1 includes "accessing data representing a multiple sequence alignment (MSA) of a plurality of polymer sequences." Claim 1 also includes identifying one or more evolutionarily conserved positions within the MSA using the recited equation.

a.   "accessing data"

The Office questions how this step occurs. For example, the Office asks, "what polymers are selected, on what basis are they selected, and how are they aligned in a multiple sequence alignment?" March 2004 Action at p. 3.

As Applicants explained in their December 2003 response, and as the Office concedes on page 4 of the Action, Applicants are not claiming **the creation** of an MSA. Instead, Applicants

are claiming accessing **existing** data representing an MSA of a plurality of polymer sequences.

As such, the Office's questions are not understood. **Any MSA** of a plurality of polymer

sequences **that exists** (whether at the time the application was filed, now, or in the future) may

be accessed consistent with claim 1. As the specification explains:

> Any polymer of monomers may be analyzed with the inventive methods.
> Application of the inventive methods is not limited to biological sequences, as it
> may be applied to chemical polymers, drugs, and other compounds.

Page 29, line 29 – page 30, line 2.

b. "identifying one or more evolutionarily conserved positions"

In addition to "accessing data," claim 1 recites:

(b)   identifying one or more evolutionarily conserved amino acid positions within the
MSA using the following equation:

$$\Delta G_i^{stat} = kT^* \sqrt{\sum_x \left(\ln \frac{P_i^x}{P_{MSA}^x} \right)^2}$$

wherein:

> i is a position in the MSA;
>
> ΔG_i^{stat} is the conservation energy value for position i;
>
> P_i^x is the probability of monomer x at position i;
>
> P_{MSA}^x is the probability of monomer x in the MSA; and
>
> kT* is an energy unit, where k is Boltzmann's constant.

In judging enablement, this step must be read in conjunction with the specification, which

explains:

> "Evolutionarily conserved amino acid positions" refers to particular positions
> within a multiple sequence alignment which display a non-zero ΔG^{stat} as
> calculated by Equation 4.

Specification at page 16, lines 6-8. The specification provides an example (see, e.g., pages 25

and 26) that involves the use of the claimed equation on the PDZ protein family. The

specification also provides source code on pages 41-53 pertaining to the use of the claimed

equation. Moreover, the specification explains that the methods disclosed will also work on any

polymer of monomers:

> Any polymer of monomers may be analyzed with the inventive methods.
> Application of the inventive methods is not limited to biological sequences, as it
> may be applied to chemical polymers, drugs, and other compounds.

Page 29, line 29 – page 30, line 2.

> In the face of these enabling teachings from Applicants' specification, the Office asserts:

> Applicant does state that this method is applicable to **any** polymer, including
> drugs, chemical polymers etc. However, Applicant does not provide any specifics
> as to how this is performed and the specification is devoid of any information
> showing an alignment of chemical or other polymers and how these types of
> polymers would be used in said invention. The specification only points to a
> limited example using the PDZ **protein** family.

March 2004 Action at p. 4 (emphasis in original). This assertion is legally insufficient. It does

not carry the Office's burden of providing **evidence** or **reasoning** why the claimed equation

cannot be applied to MSAs of polymer sequences other than the PDZ protein family. *In re*

Marzochhi, 439 F.2d 220, 224 (CCPA 1971) ("[I]t is incumbent upon the Patent Office . . . to

explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to

back up assertions of its own with acceptable evidence or reasoning which is inconsistent with

the contested statement."). The efficacy of the claimed equation is independent of the type of

data to which it applies, provided that data comprises an MSA of a plurality of polymer

sequences. Nothing in the Office's arguments refutes this.

Given its lack of evidence or reasoning, the Office's asserted non-enablement position

may be grounded in personal opinion. If so, this too is improper. *See* MPEP § 2164.05 at 2100-

184 (Rev. 1, Feb. 2003) ("The examiner should **never** make the [enablement] determination

based on personal opinion. The determination should always be based on the weight of all the

evidence.") (emphasis in original); *cf.* MPEP § 2144.03 at 2100-133 ("It is **never appropriate** to rely solely on common knowledge in the art without evidentiary support in the record as the principal evidence on which the rejection was based.") (emphasis added).

Applicants have provided an example of how to use the claimed equation on a particular polymer, and has also explained that the same equation may be used on any polymer. The Office simply has not provided any evidence or reasoning that is inconsistent with Applicant's explanation. Accordingly, the Office has not carried its burden of making a valid enablement rejection, and the rejection should be withdrawn.

2. Claim 10

Claim 10 includes "accessing data representing a multiple sequence alignment (MSA) of a plurality of polymer sequences." Claim 10 also includes calculating a conservation energy value for each position in the MSA using a recited equation. Claim 10 further includes "identifying one or more positions in the MSA that have statistically significant conservation energy values." Support for the meaning of "statistically significant conservation energy value" may be found on page 17 of the specification at lines 14-19.

Claim 10 is enabled for substantially the same reasons as claim 1. Although the two claims differ in scope, the teachings and examples from the specification that are cited above with respect to claim 1 apply with equal force to claim 10. The Office's lack of evidence or reasoning for its position is also equally insufficient as applied to claim 10. Accordingly, the enablement rejection of claim 10 and its dependents should be withdrawn.

C. Petition for Extension of Time

Pursuant to 37 C.F.R. § 1.136(a), Applicant petitions for an extension of time of one month up to and including July 12, 2004 in which to respond to the Office Action mailed

March 12, 2003. A check covering the process fee for the requested extension is enclosed. If the check has been inadvertently omitted, or if any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included, the Office is authorized to deduct or credit the appropriate fees from or to Fulbright & Jaworski Deposit Account No.: 50-1212/UTSD:645US/MTG.

D.   Conclusion

Claims 1-18 are in condition for allowance. Should Examiner Clow have any questions, comments, or suggestions relating to this application, she is invited to contact the undersigned attorney at (512) 536-3031.

Respectfully submitted,

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